DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Minneapolis District
240 Hennepin Avenue
Minneapolis MN 55401-1999
Telephone: 612-334-4100

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PURGED RAH

January 14, 1999

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Refer to MIN 99 - 14

C. Ray Holman
Chairman and Chief Executive Officer
Mallinckrodt, Inc.
675 McDonnell Boulevard
St. Louis, Missouri 63134

Dear Mr. Holman:

During our recent inspection of your Mallinckrodt Nellcor Puritan Bennett medical oxygen transfilling operation located at 2600 - 31st Avenue South, Minneapolis, MN, our investigators found serious violations of the current Good Manufacturing Practices (GMPs) for Finished Pharmaceuticals, Title 21, Code of Federal Regulations, Part 211 (21 CFR 211). Oxygen is a drug within the meaning of Section 201(g) of the Federal Food, Drug and Cosmetic Act (the Act). These violations cause your transfilled oxygen to be adulterated within the meaning of Section 501(a)(2)(B) of the Act.

The violations observed during our inspection include, but are not limited to, the following:

1. Failure to have appropriate laboratory determination of satisfactory conformance to final specifications for the drug product [21 CFR 211.165(a)] in that:

(A) There is a lack of full USP testing on Medical Air USP. One cylinder from each manifold filling sequence is not analyzed for contaminants.

(B) There is a lack of an identity test for the Helium USP on one cylinder from the manifold filling sequence for the Helium-Oxygen gas mixture.

2. Failure to calibrate instruments, apparatus, gauges, and recording devices at suitable intervals in accordance with an established written program [21 CFR 211.160(b)(4)] in that you are not following your SOP ~~~~ Model 570A Gas Analyzer" because the oxygen analyzer is not calibrated each time it is turned on. Also, the operator's manual for the 570A states the battery voltage is to be checked after the oxygen analyzer is turned on and before calibration.

3. Failure to have written procedures for production and process control designed to assure that the drug products have the identity, strength, quality and purity they purport or are represented to possess [21 CFR 211.100(a)] in that your SOP "Medical Air System" does not specify how the air filter should be cleaned or when to replace it.

The above indication of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Good Manufacturing Practice regulations. Federal agencies are advised of the issuance of all Warning Letters about drugs so they may take this information into account when considering the award of contracts.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Possible actions include seizure and/or injunction. This is official notification that FDA expects all your locations to be in compliance.

In addition, further review of the collected records reveals:

* You are not performing the Carbon Monoxide (CO) test as required by the USP. Your batch records have an "X" in the box for the CO test. According to your batch records "X" indicates the action is not required.

* Batch record 11919 was reviewed and approved by the person performing the filling. It appears the same person also issued, used and returned labels. This is in violation of 21 CFR 211.125, failure to have strict control over labeling issued for use in drug product labeling operations.

Review of labeling from the previous inspection reveals your Oxygen USP label lacks the "Caution: Federal law prohibits dispensing without a prescription" statement. Labeling for drugs is now required to bear, at a minimum, "Rx Only." Failure to include this on your label misbrands your product.

We have also reviewed your response dated December 28, 1998, to the form FDA-483 that was issued to your firm on December 16, 1998. The responses to observations 4 and 6 are adequate. We do not require a Certificate of Analysis (COA) with all shipments of medical gases. However, if a valid COA is NOT received, then full USP testing is required.

Concerning the lack of an identity test for Helium USP, your Branch Manager agreed that the identity test was not performed and "OK" meant the other gas was Helium. However, after the inspection he recanted his statement. This would indicate either you are not performing the identity test for Helium or Mallinckrodt Nellcor Puritan Bennett has not properly trained its personnel.

With regards to turning on/off/on/off, etc., without re-calibration or checking the battery of the ~~~~ during the day, our investigators observed this practice many times, not just the one time when the customer was unable to observe the reading. This indicates the turning on/off, etc. without recalibration or checking the battery of the ~~~~ throughout the day is general practice and not an isolated incident.

Your responses will be made part of the official file for your firm and promised corrections will be verified during the next inspection.

You should notify this office in writing within 15 working days of receipt of this letter of specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, state

the reason for the delay and the time within which the corrections will be completed.

Your reply should be sent to Compliance Officer Carrie A. Hoffman at the address indicated on the letterhead.

Sincerely,

James A. Rahto
Director
Minneapolis District

CAH/ccl

xc: John C. Rukavina
Branch Manager
Mallinckrodt Nellcor Puritan Bennett
2600 - 31st Avenue South
Minneapolis MN 55406